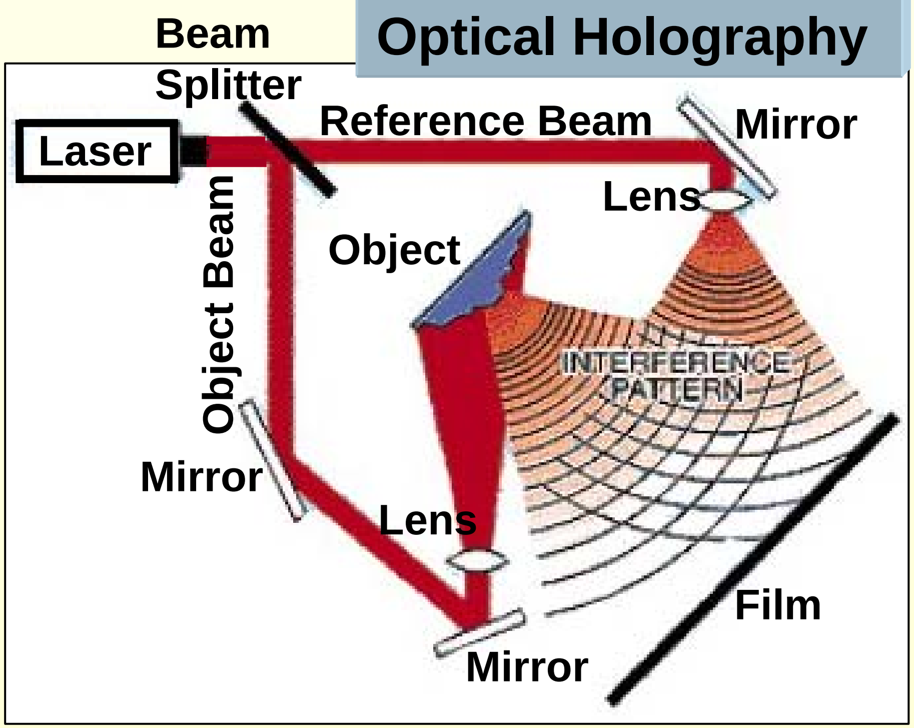
Prospective Applications of Neutron Holography in Biology

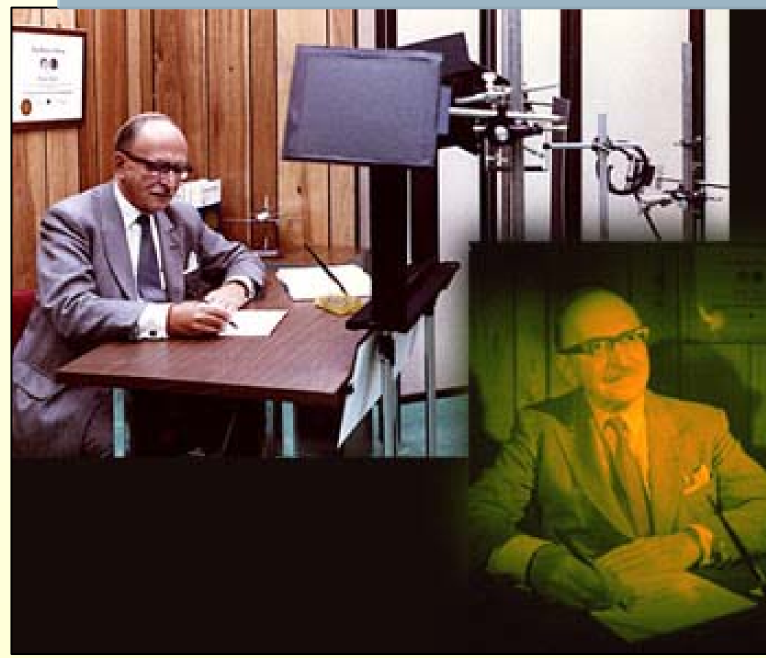
J. Katsaras, R.B. Rogge and B. Sur

Optical Holography

Optical Holography



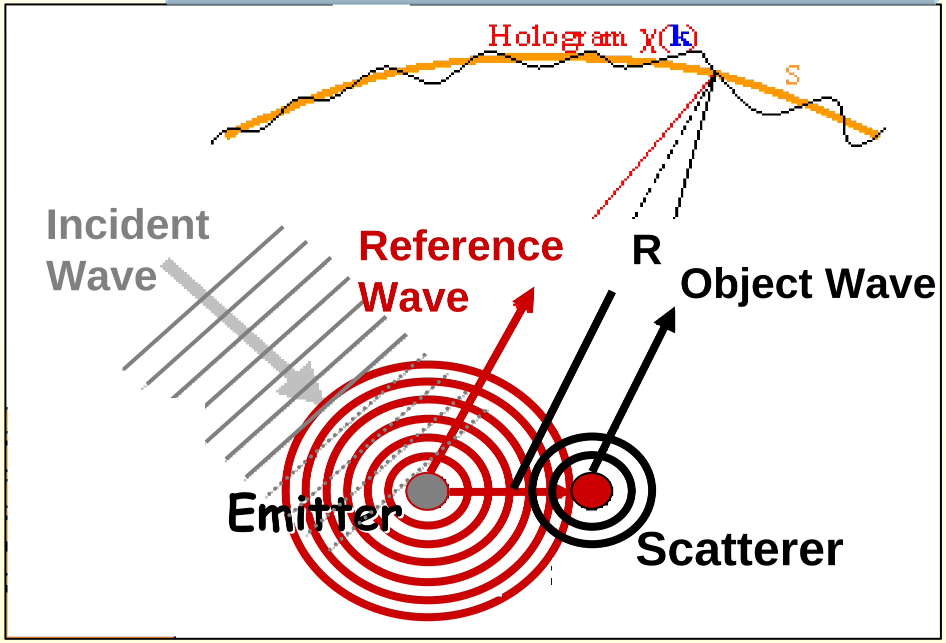
Dennis Gábor (1900-1979)



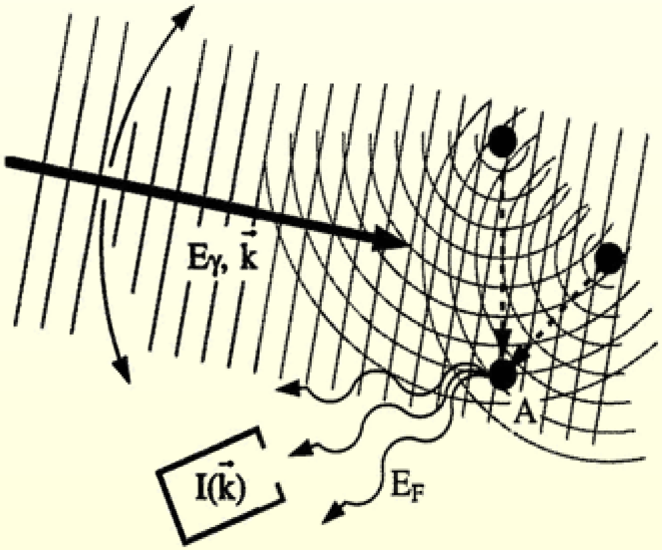
Holography was not realized until 1963!

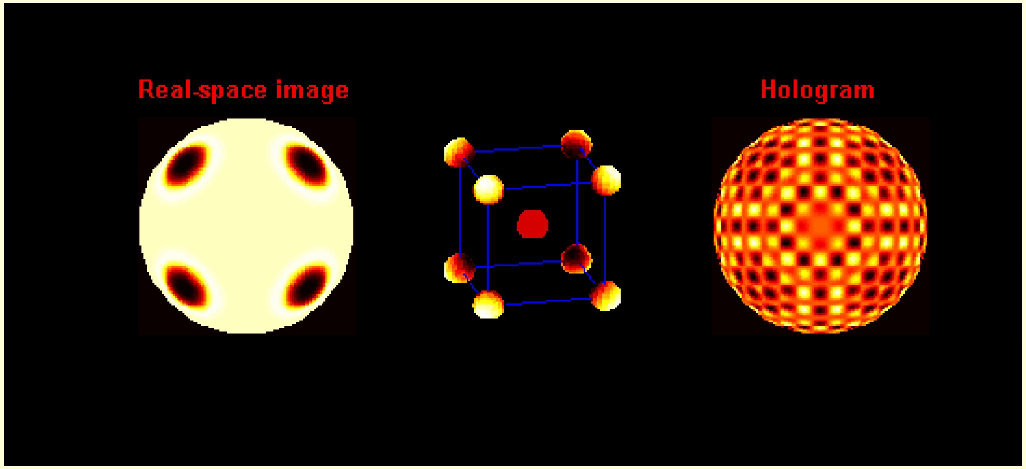
Atomic Resolution Holography

"Inside Source" Holography



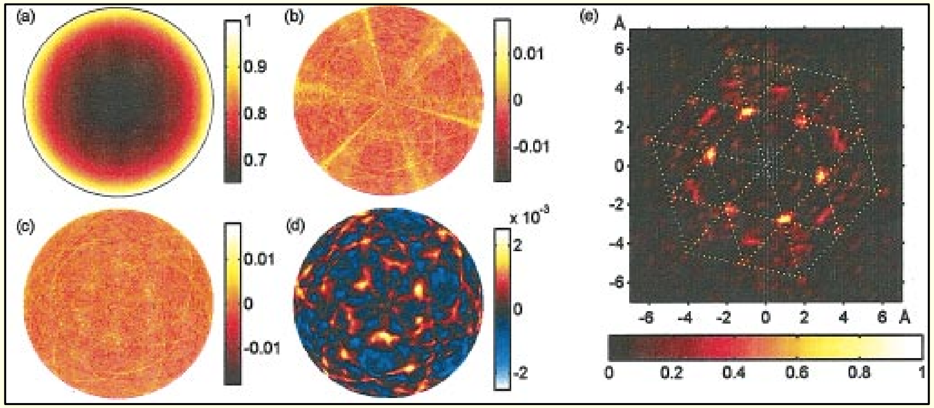
"Inside Detector" Holography

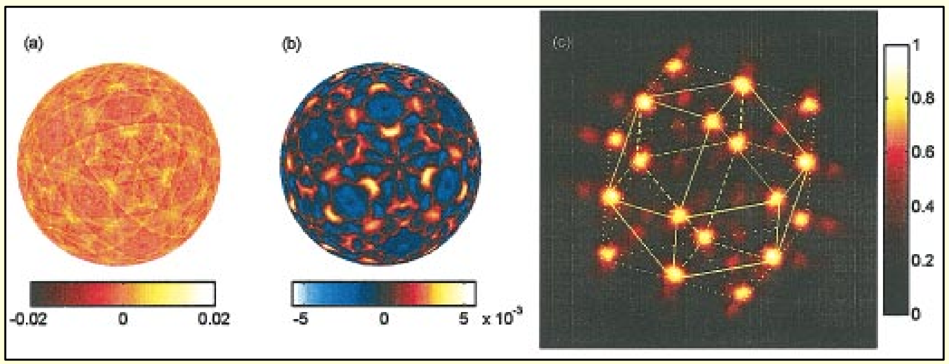


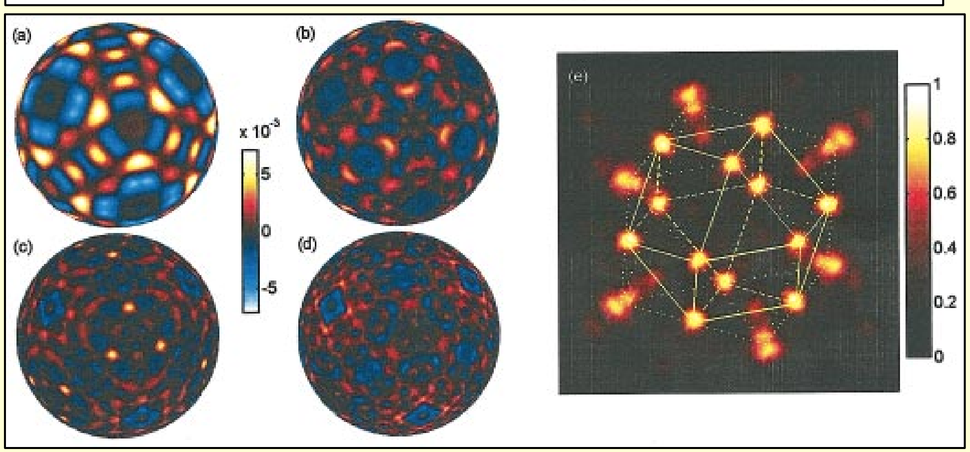


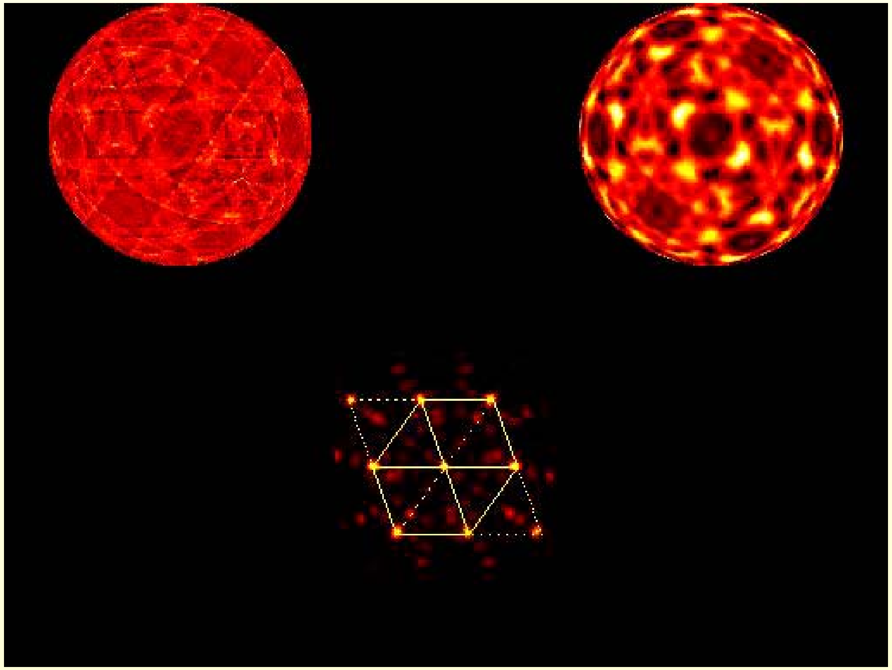
Faigel and Tegze
Rep. Prog. Phys. **62** (1999) 355–393

In 1986 Szöke extended visible light holography to x-ray and electron diffraction experiments.





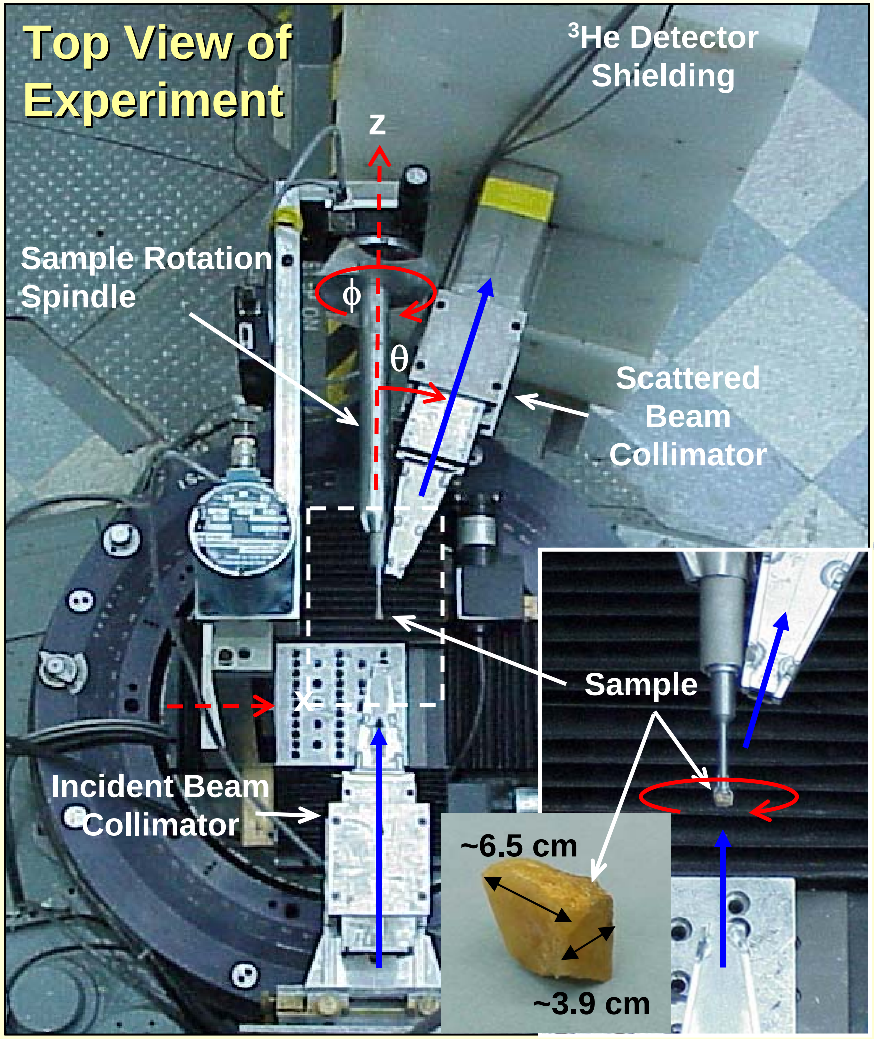


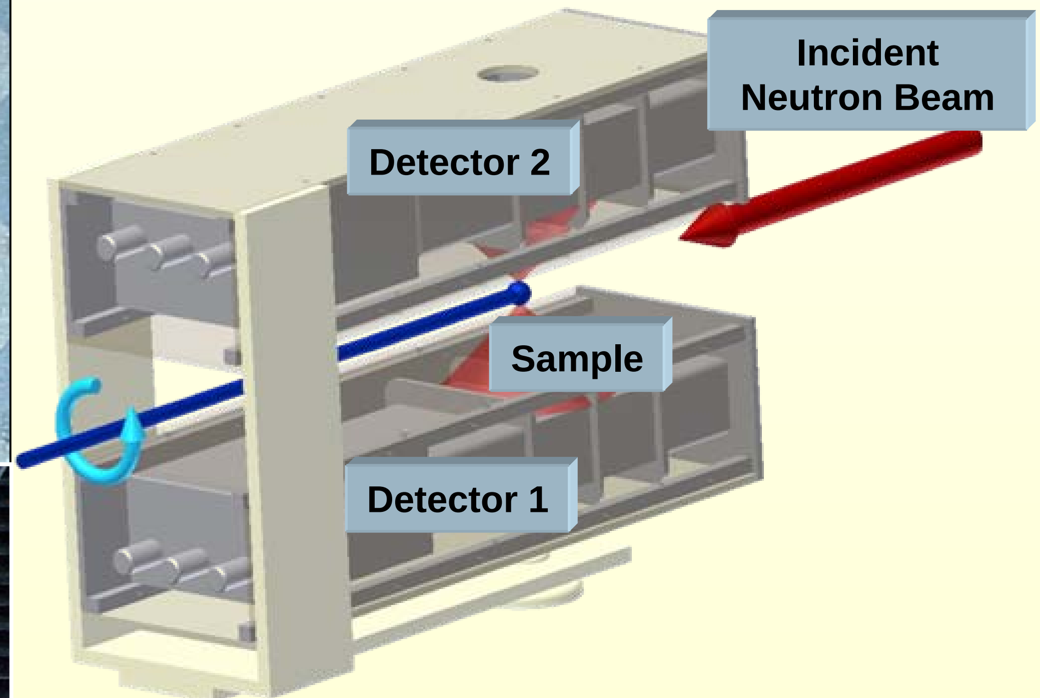


Tegze et al., Phys. Rev. Lett. 82, 4847 (1999)

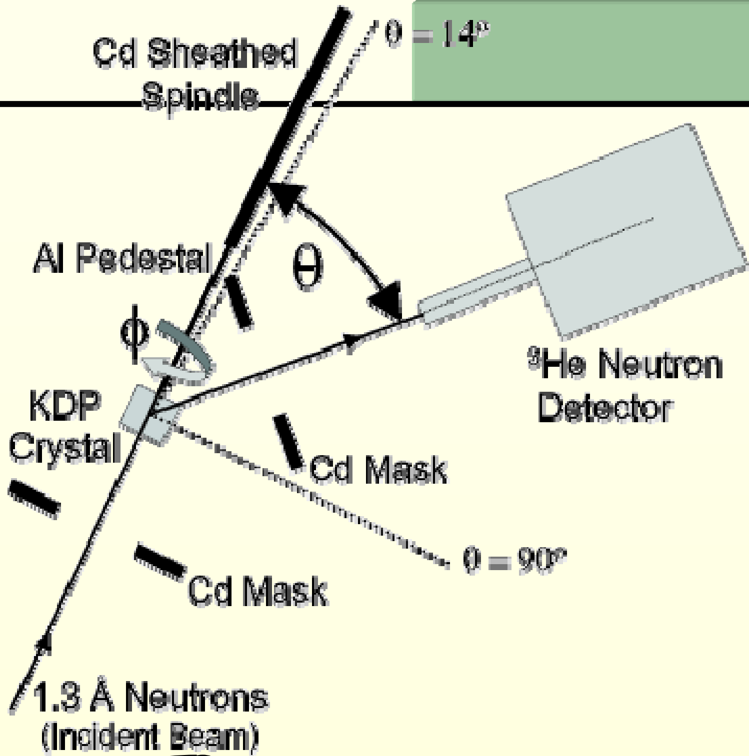
National Research Universal, Chalk River

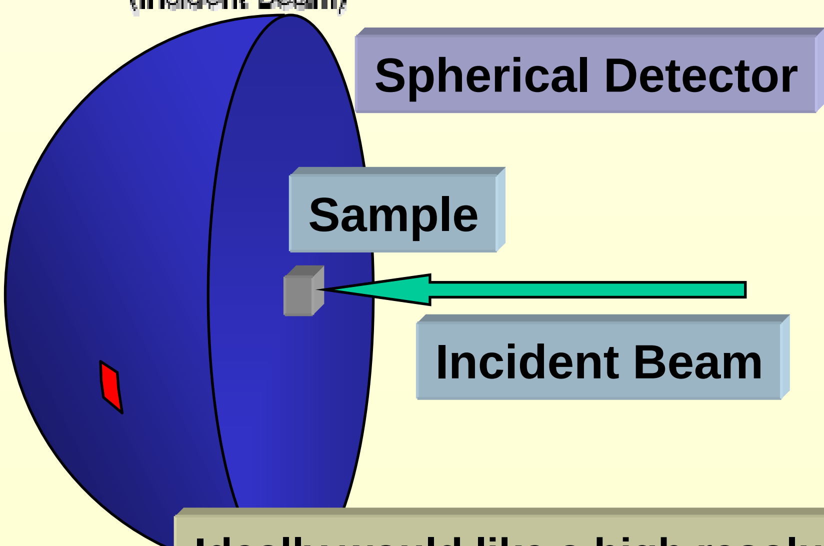
Inside Source and Detector Geometries



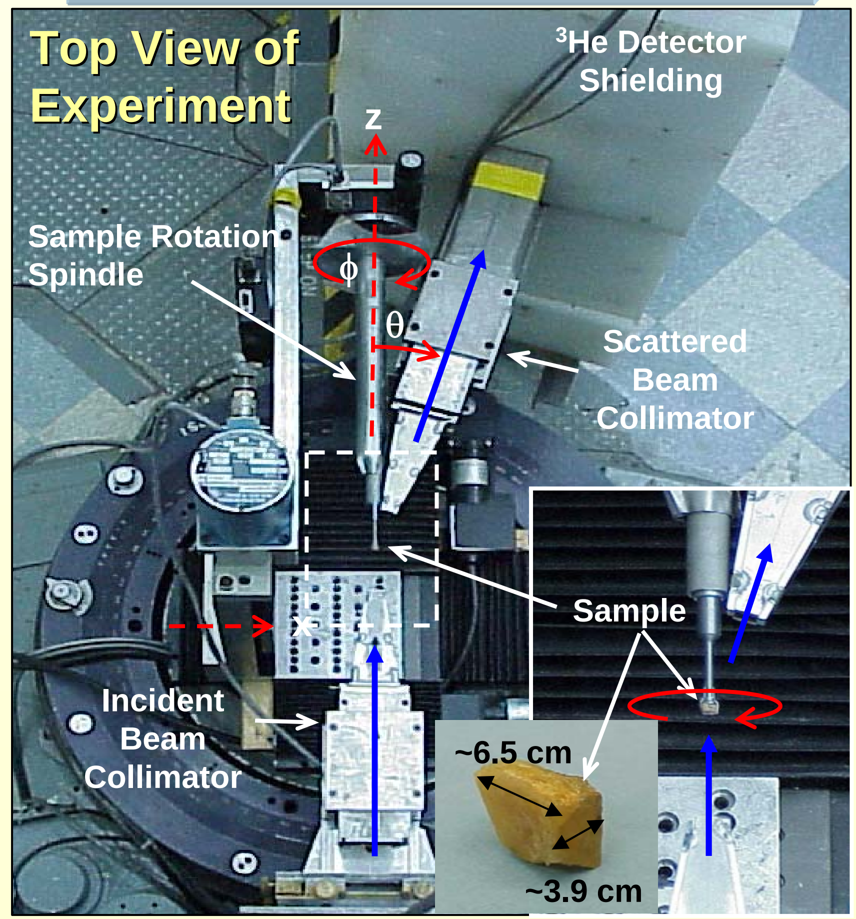


ISG – Observation of K-Lines





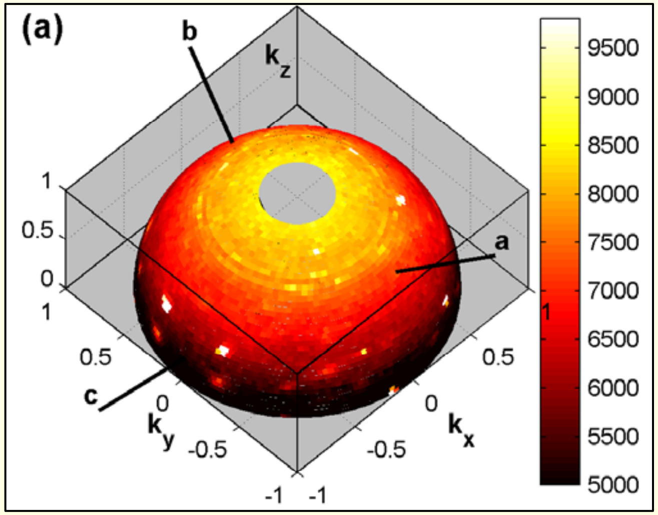
Brute Force Method
Map out sphere pixel by pixel
(5023 pixels at 2° × 2°)



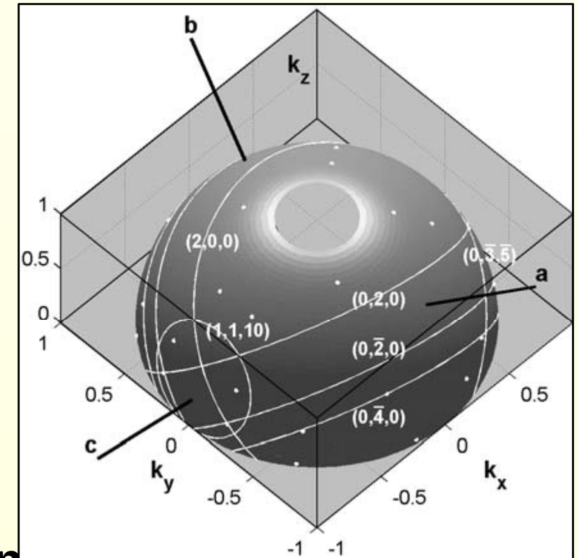
Scott Ecrit (Canadian Museum of Nature)

Ideally would like a high resolution spherical imaging detector.

ISG – Observation of K-Lines

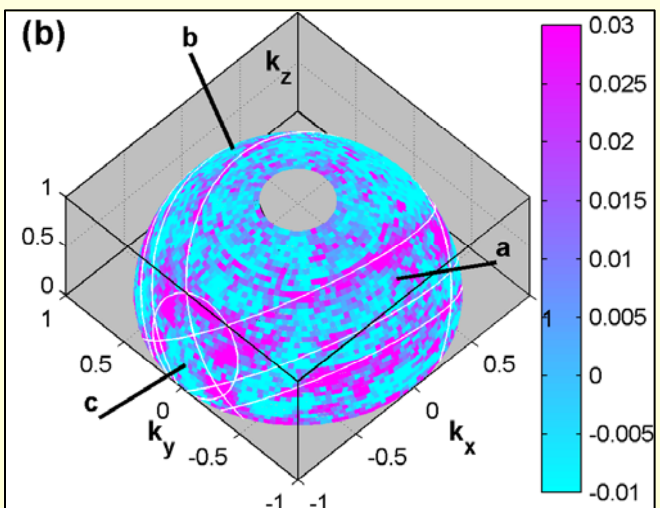


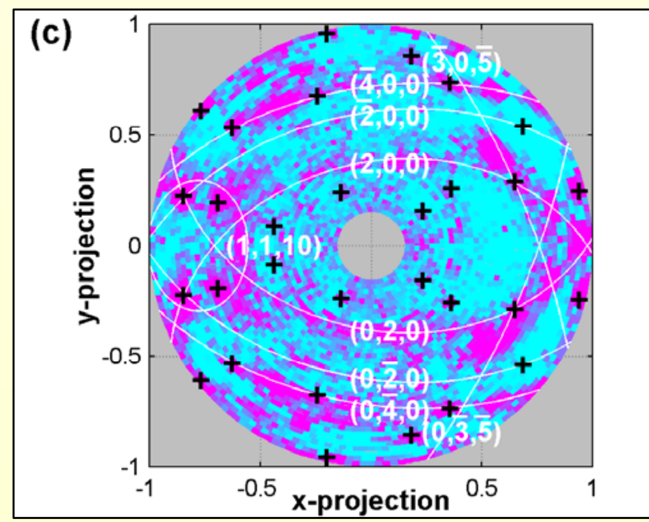
Single crystal <u>KDP</u> KH_2PO_4 at λ = 1.3 Å



Intensity modulation

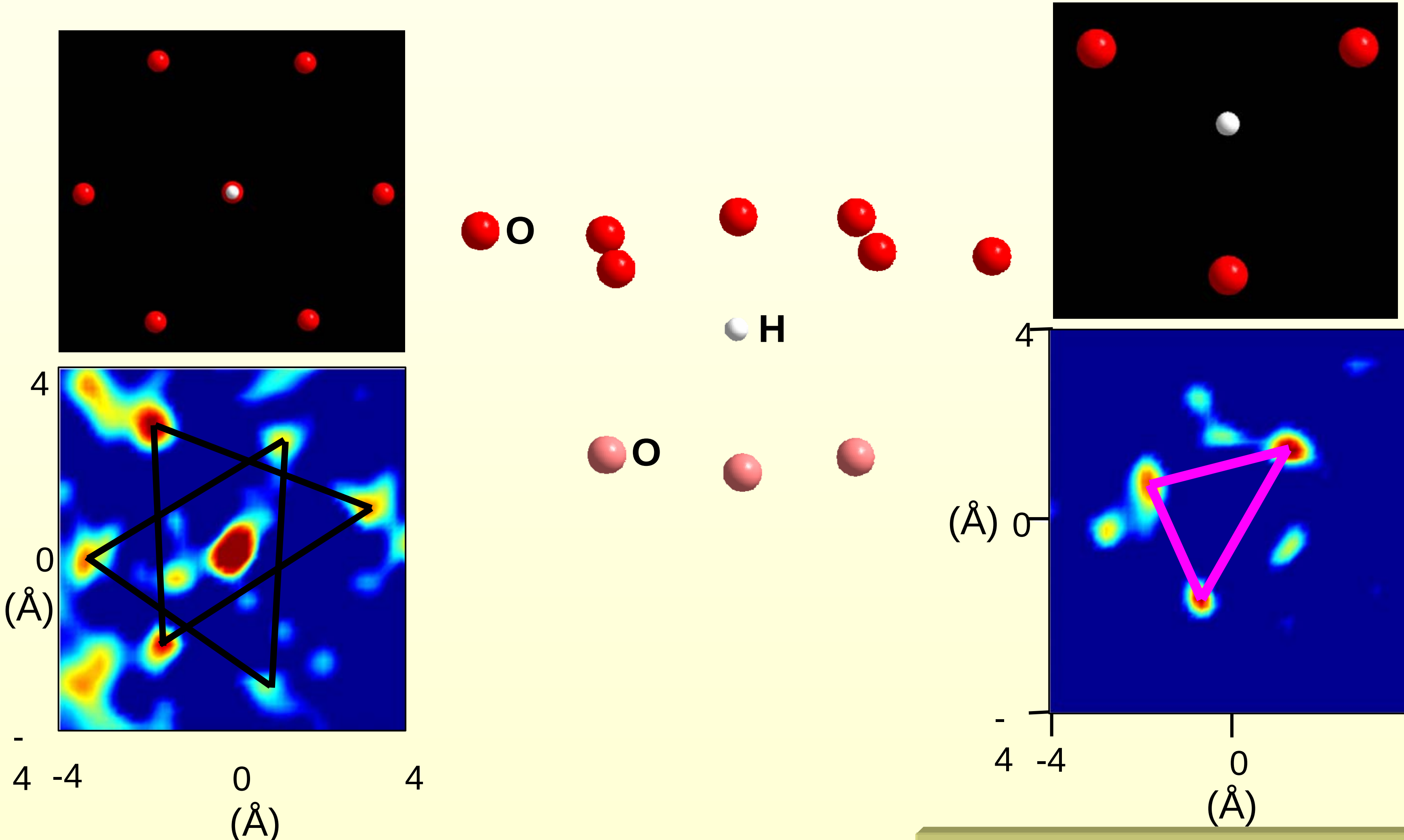
corrected for background, self-attenuation, Debye-Waller factor etc.





B. Sur et al., Phys. Rev. Lett. <u>88</u>, 065505 (2002)

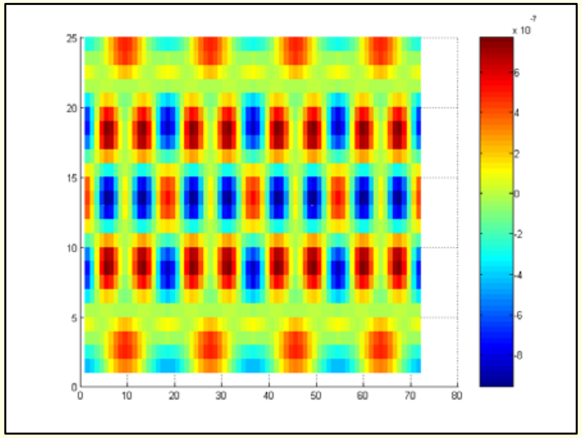
Reconstruction of Simpsonite

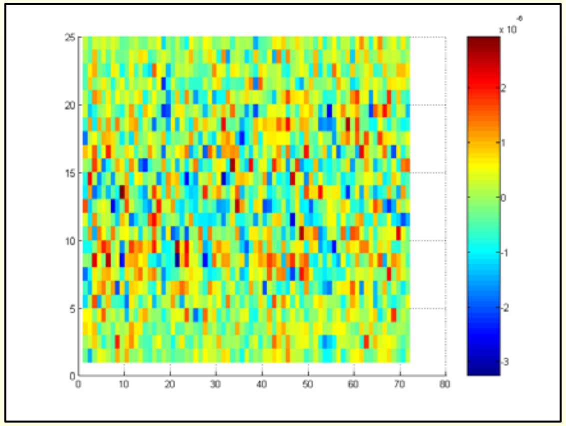


B. Sur et al., Nature 414, 525 (2001)

Hologram S/N and Real Space

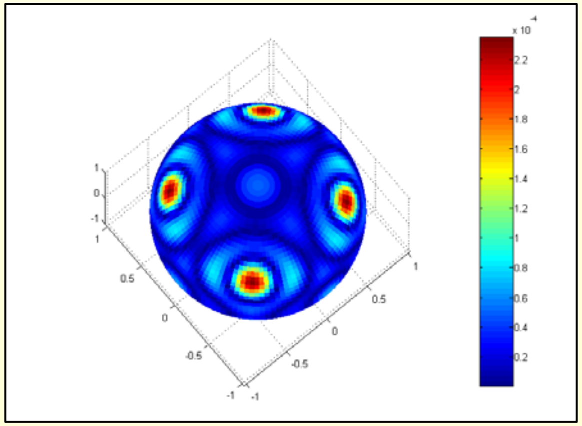
Hologram

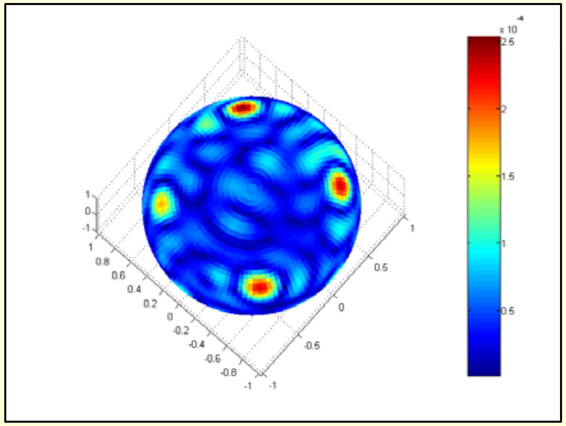




Noisy Hologram (Poisson Noise)

Structure



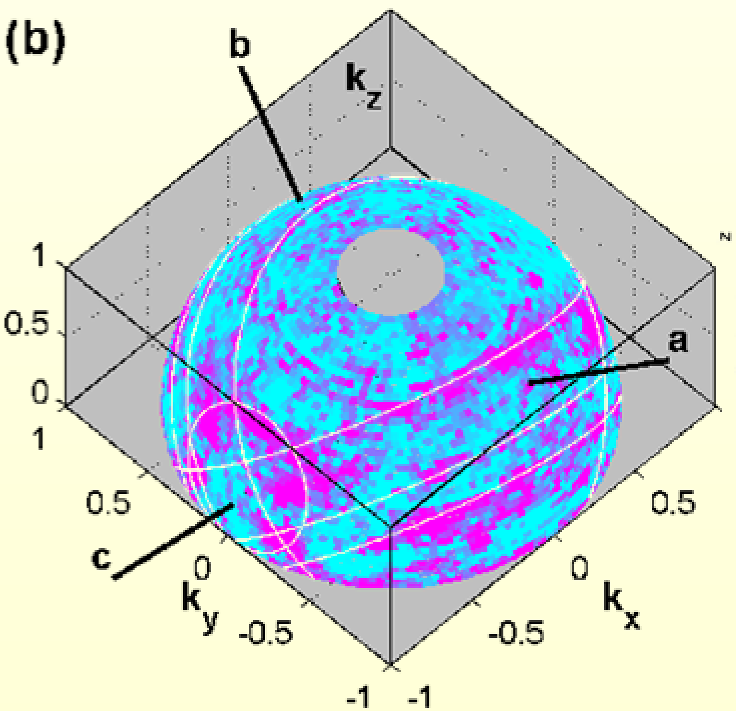


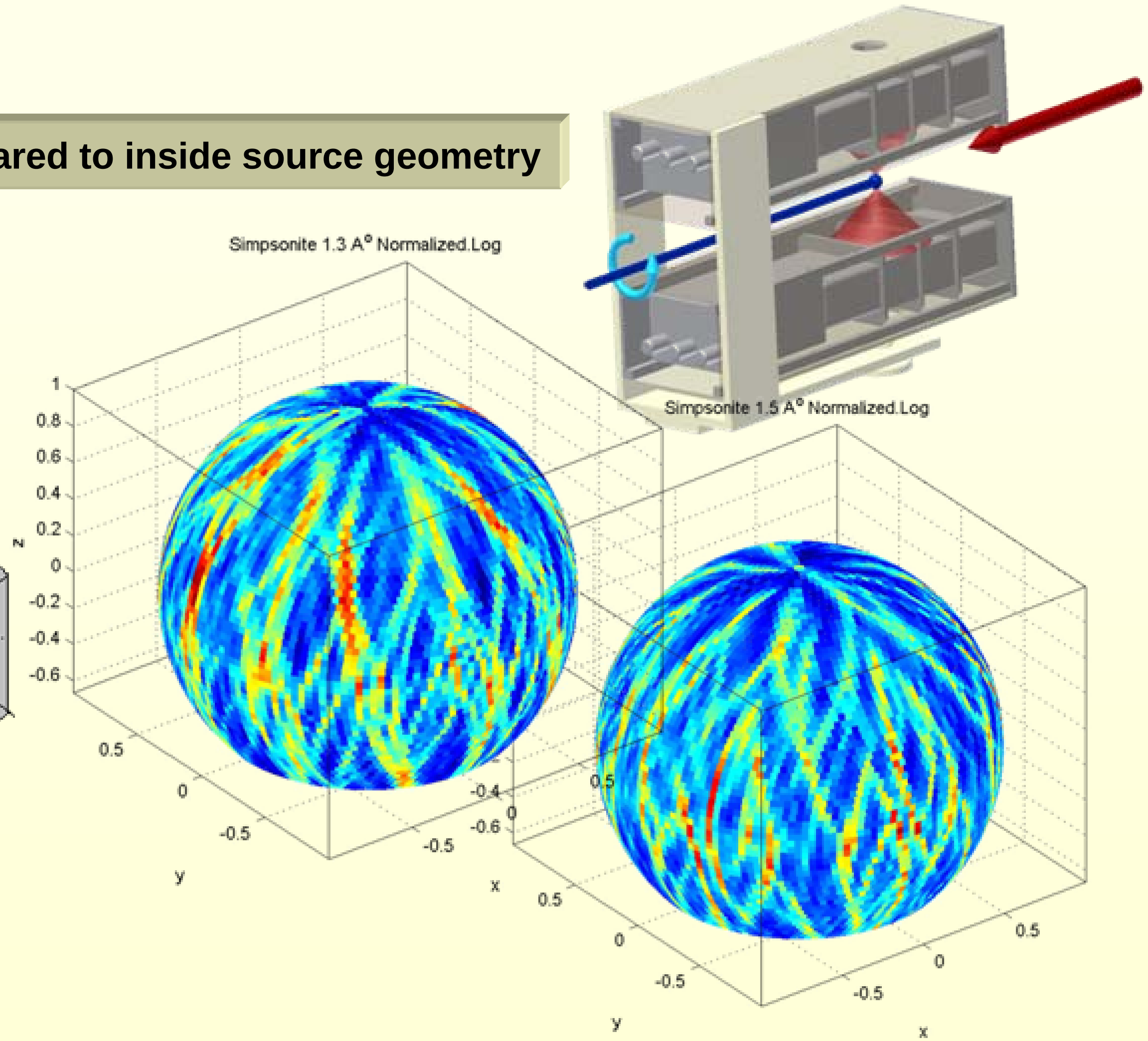
Structure

Courtesy of Márton Markó, Research Institute for Solid State Physics and Optics, Hungary

IDG – Simpsonite1.3 and 1.5 Å

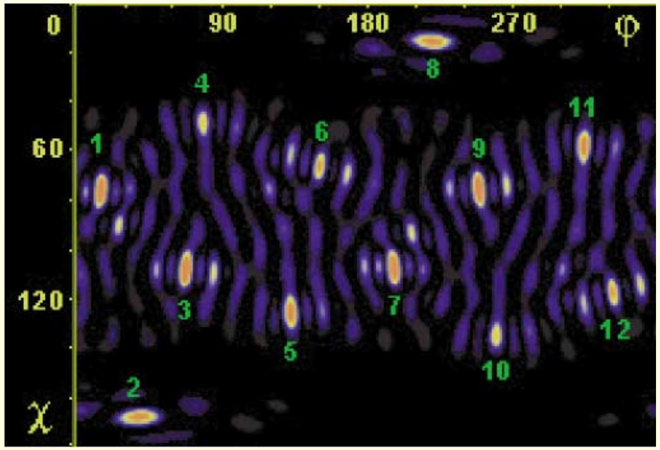
~ 400 fold increase in S/N compared to inside source geometry

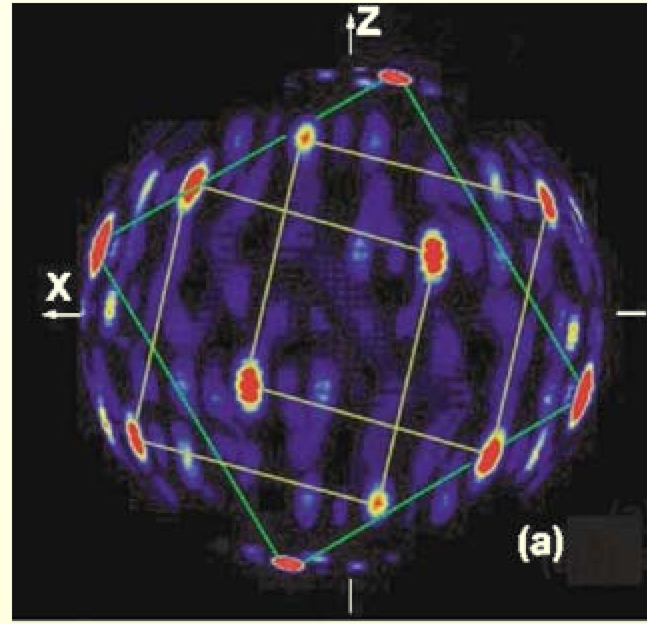




NRC·CNRC

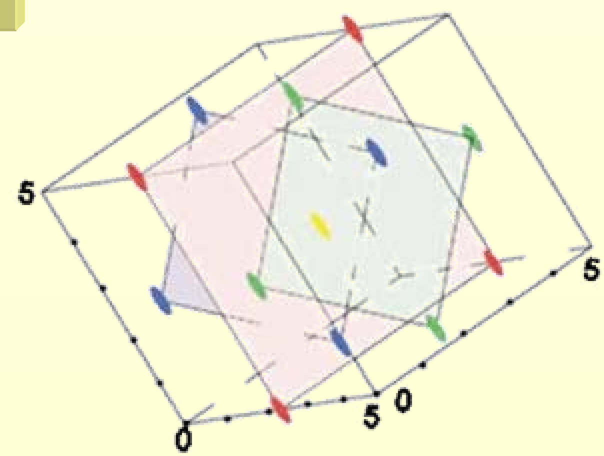
IDG – Imaging of Pb using Cd





L. Cser et al. Phys. Rev. Lett. 89, 175504 (2002)

Cser et al. have recently reconstructed a hologram which locates Pb atoms 4 shells from the origin (sumitted to Phys. Rev. Lett.)



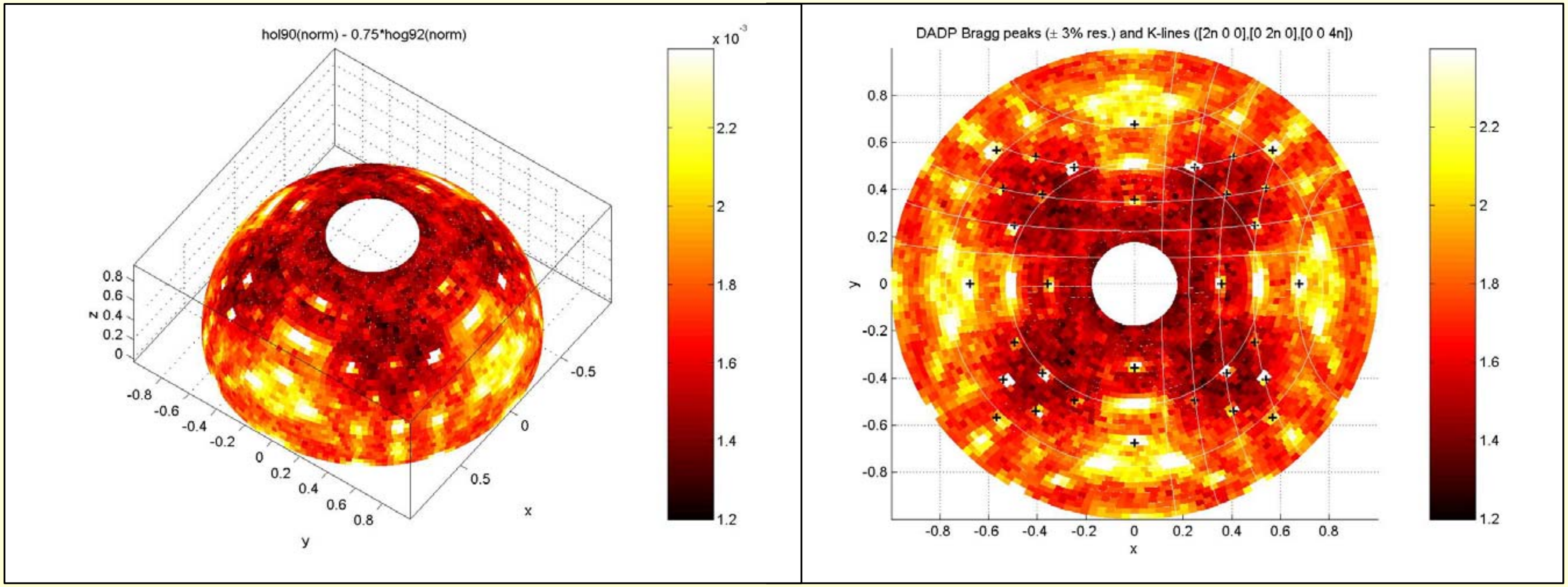
(b)

K-Lines and No H?

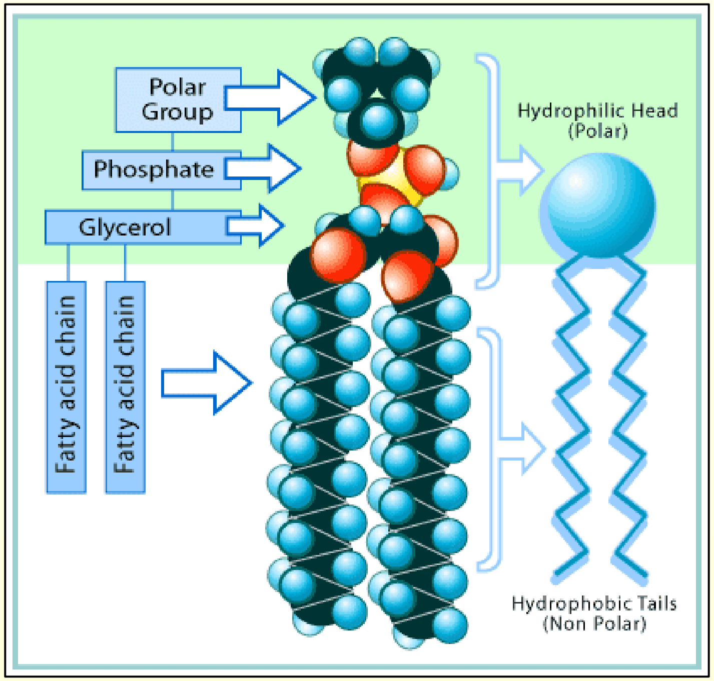
Hologram (*K*-lines) can be formed by any kind of interaction between order and disorder in the scattering system

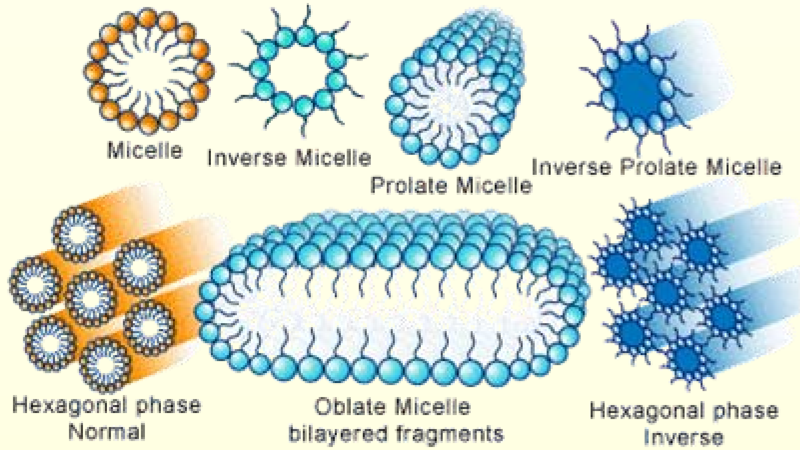
Spin incoherence (*e.g.,* hydrogen)
Isotope Incoherence
Nuclei in Interstitial Sites
Oriented Grains or Crystallites in Random Relative Locations Random Atom Movements

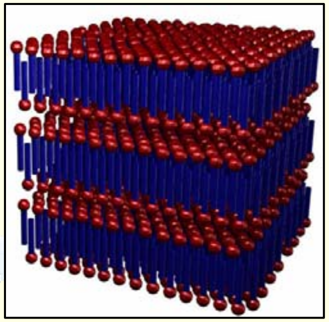
Sur *et al.*, *Phys. Rev.* B 71, 065505 (2005)

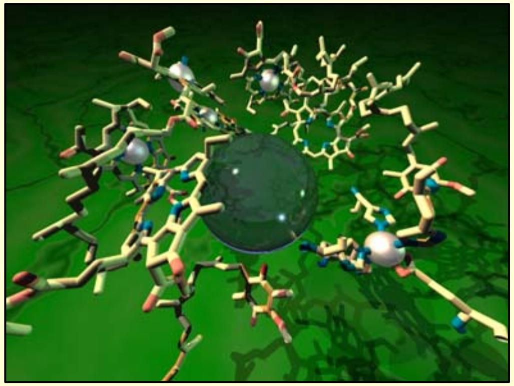


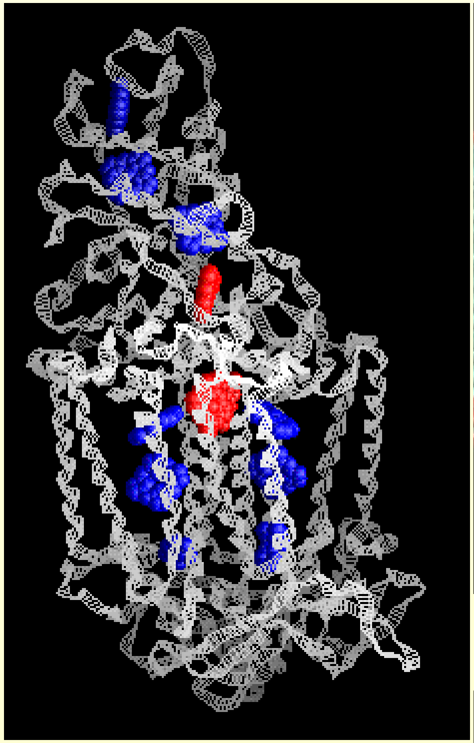
Hydrogenous Materials

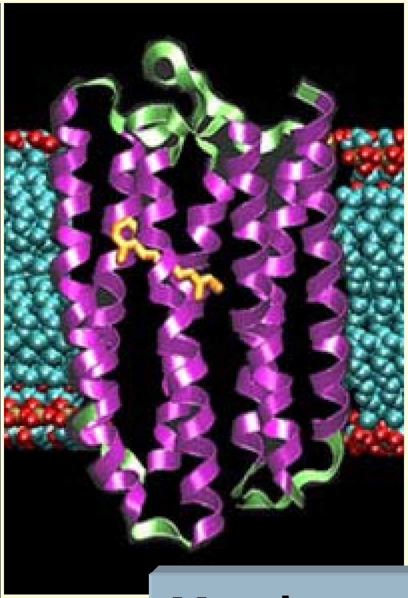






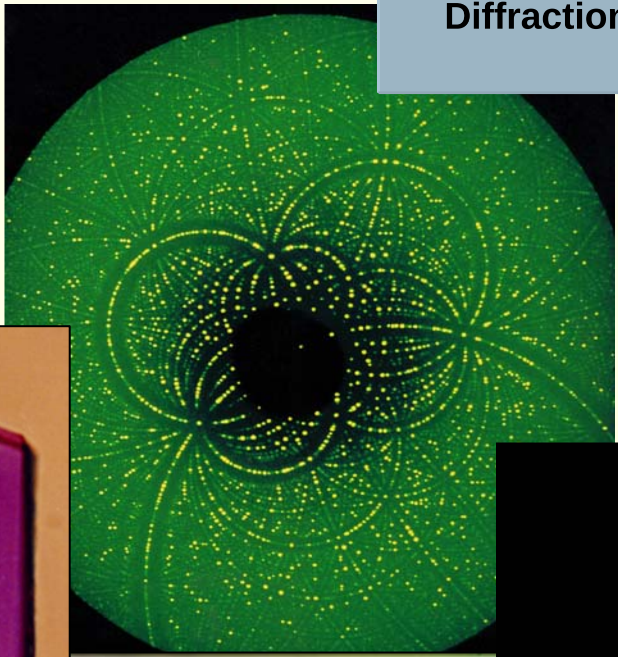




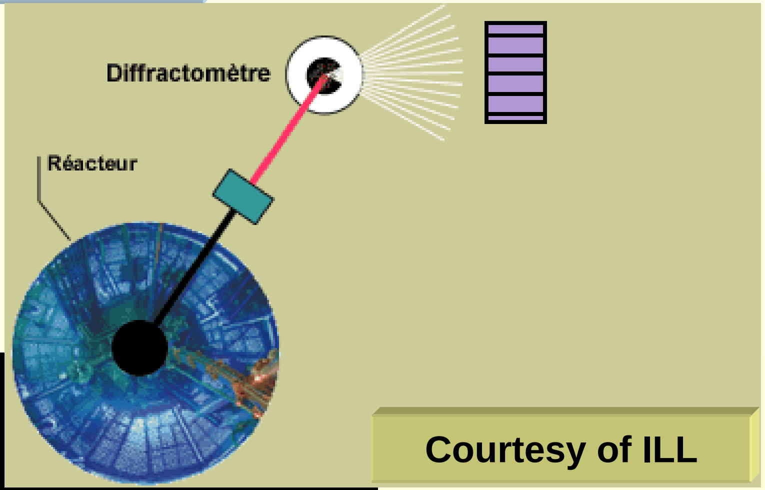


Membrane Proteins

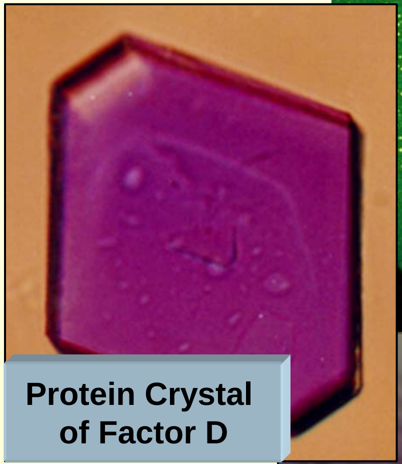
Protein Crystallography – 3D Structure



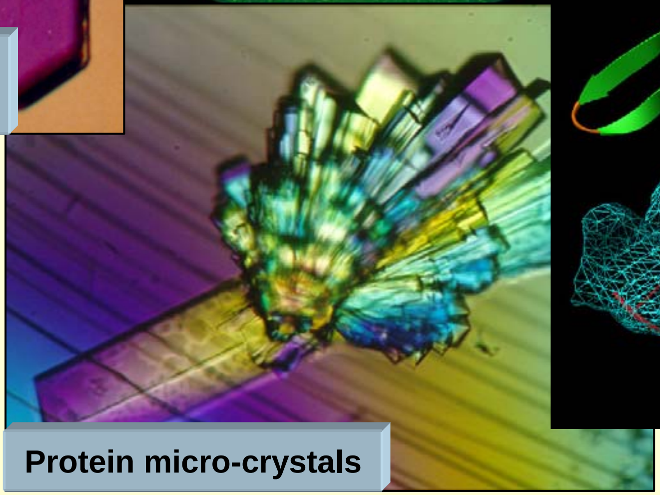
Diffraction pattern of protein crystal



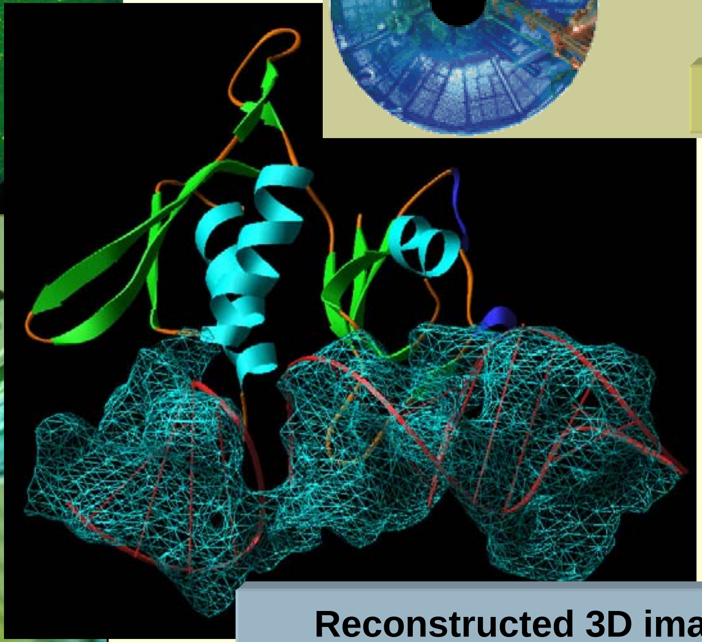
Courtesy of ILL



Protein Crystal of Factor D

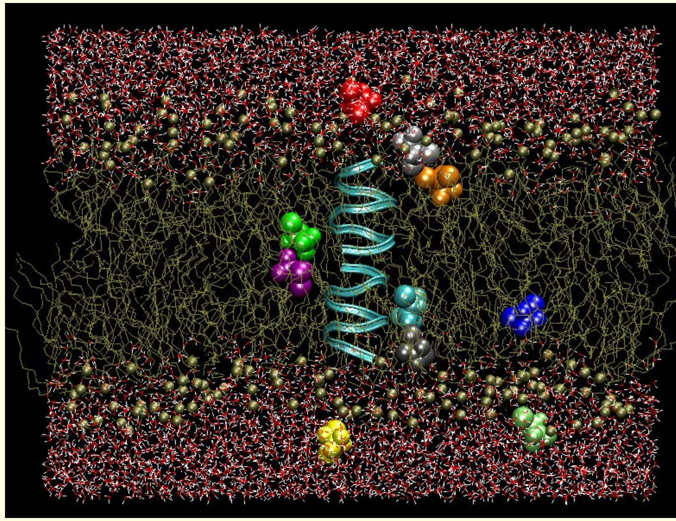


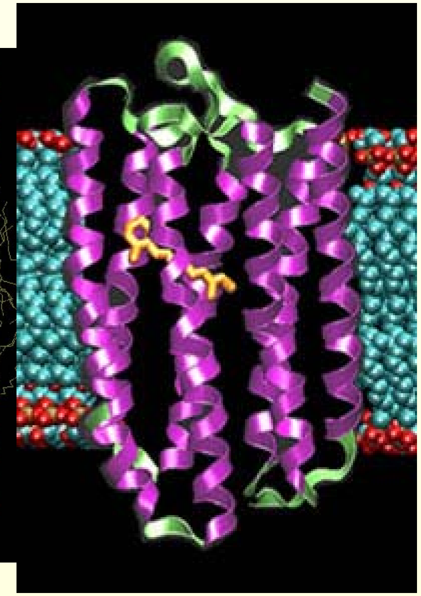
Protein micro-crystals

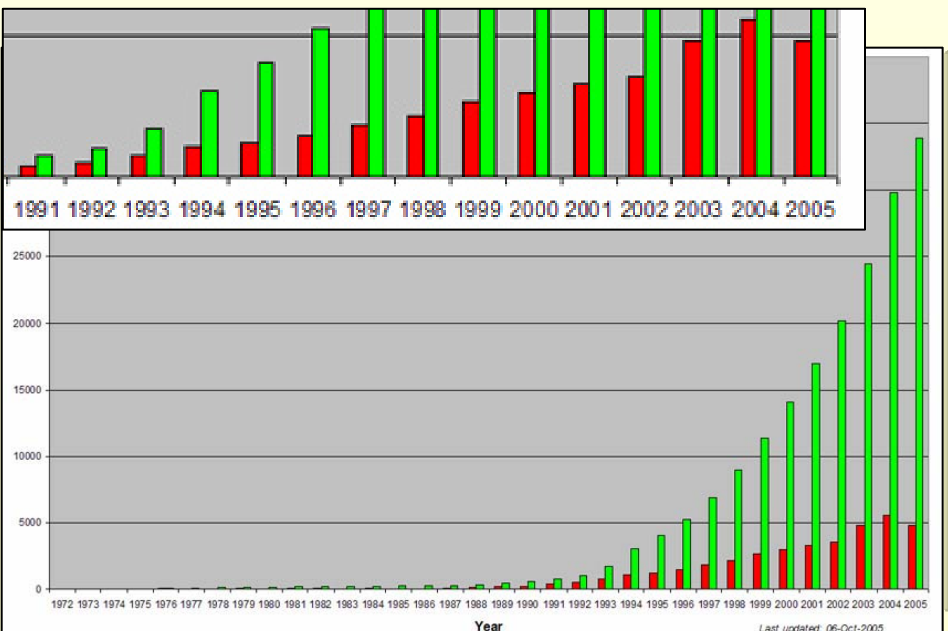


Reconstructed 3D image of ribosome from diffraction pattern

1/3 of All Proteins – Only 100 Structures



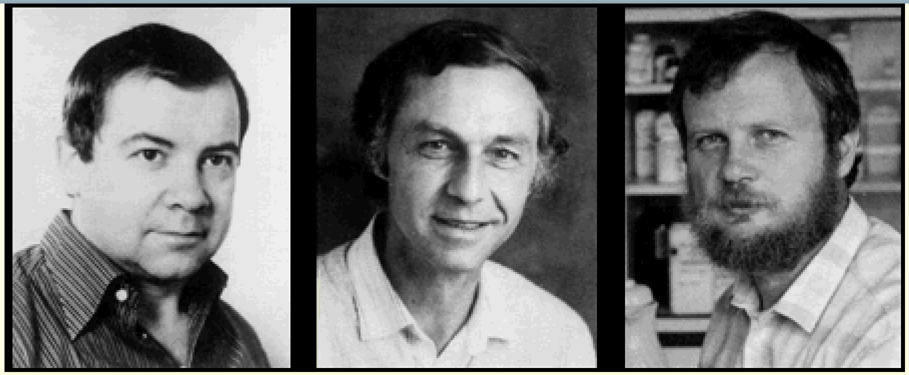


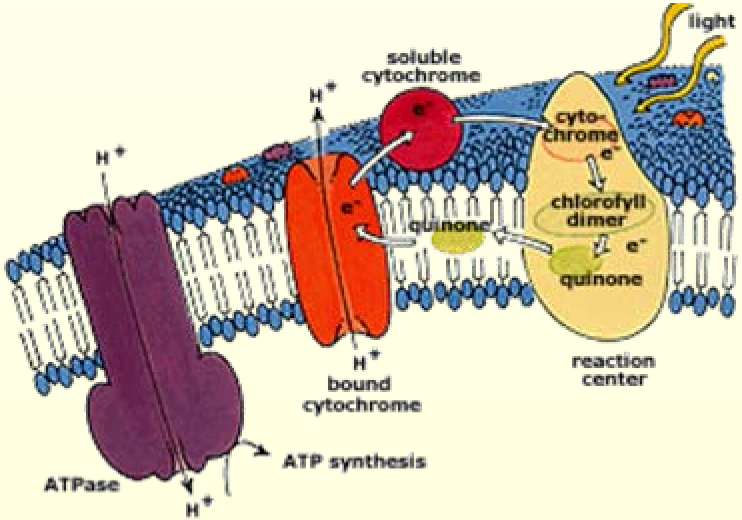


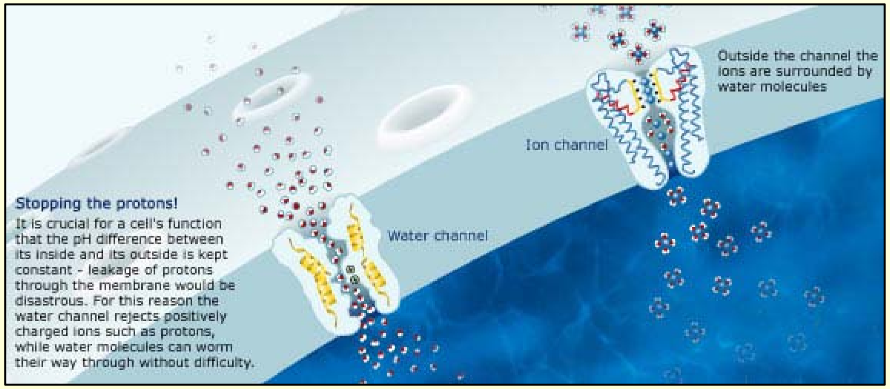
- **Membrane associated proteins are known to constitute approximately one third of all known proteins.**
- **Of the ~34,000 3D protein structures, only 100, or so, are of membrane proteins (Research Collaboratory for Structural Bioinformatics).**
- **The primary reason for this scarcity of membrane protein structures is that integral proteins are not easily crystallized by standard techniques, and tend to aggregate in the course of crystallization from solution.**

Membrane Protein Structure - High Impact

3D Structure of the Photosynthetic Reaction Center
1988 Nobel Prize Chemistry - J DEISENHOFER, R HUBER & H MICHEL





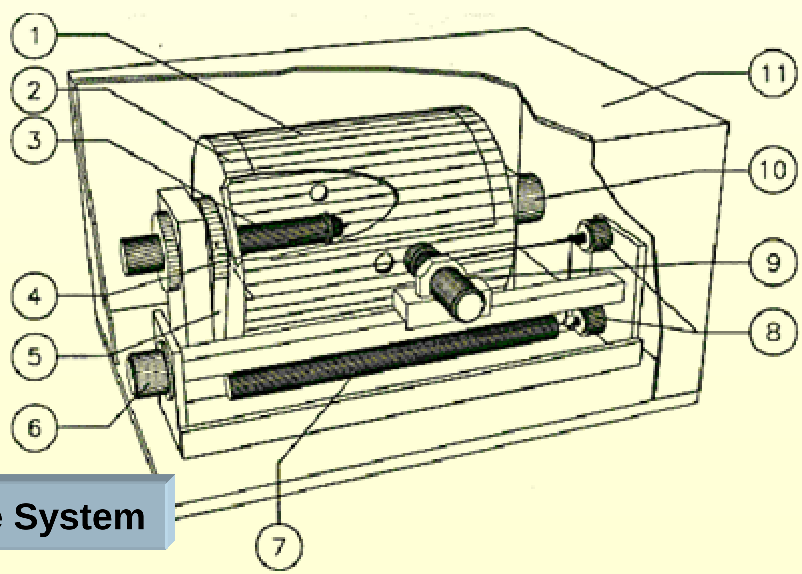


Discovery of Water Channels and 3D Structure of Ion Channels
2003 Nobel Prize in Chemistry
R. MacKinnon and P. Agre

Points of Discussion

- Can we realistically reconstruct samples containing multiple incoherent scatterers, i.e. proteins?
- There are many “poor quality” protein crystals (i.e., diffract to ~ 10 $Å^{-1}$) suitable for holography. Can we solve this class of crystals to atomic resolution?
- The phase problem for large structures is still a considerable obstacle for crystallographers. Requires the production of various crystals (i.e., isomorphous replacement). With holography we can solve the structure from one single crystal and a number of wavelengths.
- Can we use the LADI system at ILL to collect complete data in hours instead of days?
- Can we put together a working group that will make headway in addressing ONE important problem?

1: Image plate on drum. 2: Drum. 3: Sample holder. 4: Crystal. 5: Transmission belt to drive drum. Motor is under table. 6: Carrier for reading head with photomultiplier. 7: He-Ne laser. 8: Mirrors for bringing the laser light to the reader head. 9: Reader head with photomultiplier. 10: Encoder for drum rotation. 11: Cover.



LADI Image Plate System

One Proposed Strategy

- Start with “poorly” crystalline sample i.e. diffracts to ~ 6 Å resolution
- Solve structure using X-Ray diffraction
- Carry out Neutron/X-ray holography
- Take the low resolution X-ray structure and fit hologram i.e. calculate hologram and refinement data
- Result should be atomically resolved structure

Spallation Neutron Source

Recent Neutron Holography Papers

Cser et al., *Europhys. Lett.* <u>54</u>, 747 (2001).

Sur et al., "Atomic Structure Holography Using Thermal Neutrons", *Nature* <u>414</u>, p.525 (2001).

Sur et al., "Observation of Kossel and Kikuchi Lines in Thermal Neutron Incoherent Scattering", *Phys. Rev. Lett*. <u>88</u>, 065505 (2002).

Cser et al., "Holographic Imaging of Atoms Using Thermal Neutrons", *Phys. Rev. Lett.,* <u>89</u>, 175504 (2002).

Sur et al., Diffraction Pattern from Thermal Neutron Incoherent Elastic Scattering and the Holographic Reconstruction of the Coherent Scattering Length Distribution", *Phys. Rev. B,* <u>71</u>, 014105 (2005).